Clinical guidelines and indications for bronchoalveolar lavage (BAL): pulmonary malignancies.

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Clinical guidelines and indications for bronchoalveolar lavage (BAL): Report of the European Society of Pneumology Task Group on BAL

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Contents

Pulmonary malignancies

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The major diagnostic techniques to obtain material for the diagnosis of cancer were, and remain direct forceps biopsy of bronchoscopically visible tumours and transbronchial biopsy for peripheral lesions.

Nevertheless, BAL can obtain material which can permit the cytological diagnosis of cancer. The criteria for the cytological diagnosis of cancer in the lung are well established [243]. However, since BAL is often performed and interpreted by pulmonologists [190] who are not trained cytologists and because the stains most often used by pulmonologists do not always reveal cytological detail, it is likely that the power of BAL to aid in the diagnosis of lung cancer has been underappreciated.

Table 1. – Examples of BAL used in the diagnosis of cancer

Type of cancer	Reference
Primary lung	
Squamous	[229, 244–248]
Adenocarcinoma	[229, 244–247]
Large cell	[229, 244, 246, 247]
Small cell	[229, 244–246]
Bronchoalveolar	[249–251]
Metastatic	
Solid tumours	[229]
Breast	[252]
Lymphangitic spread	[253, 254]
Haematological malignancy	
Hodgkin's	[255–257]
Non Hodgkin's lymphoma	[251, 256, 258, 259]
Leukaemia	[74, 229, 256]
Waldenstrom's	[260]
Myeloma	[256]
Mycosis fungoides	[261]

The exact circumstances in which lavage will be most important and the diagnostic yield comparable with other techniques are, as yet, unanswered questions. In addition, it should be recognized that BAL performed for other reasons may reveal malignant cells in cases where cancer is not suspected.

A rapidly enlarging collection of case reports and small series suggest that BAL can be of use in the diagnosis of a number of malignancies in the lung (table 1). With regard to primary lung cancers, there are six series (including unpublished data contributed by the co-authors of this document) which address the issue of diagnostic yield of BAL (table 2). Overall, the diagnostic yield was about 50% in these six series ranging from 14–69%. While the numbers available are small, the data available suggest that the diagnostic yield of BAL might be higher for bronchoalveolar cell carcinoma than for other cell types of primary pulmonary malignancy (table 3).

A high yield should also be expected in lymphangitic spread of metastatic cancer. The best technique of lavage to use for the diagnosis of cancer is unknown (table 4). It would be ideal to compare lavage with transbronchial biopsy, for example, for peripheral lesions, diffuse lesions and large central bronchoscopically visible lesions. Studies designed to address these issues are currently underway. While it is not possible to draw any firm conclusions, lavage can be of use in some cases of isolated peripheral nodules. It was also felt that lavage was particularly useful in diffuse lesions, such as those found with bronchoalveolar cell carcinoma. Thus, while lavage can clearly provide diagnostic material in a variety of clinical settings, its yield in specific settings, remains to be determined.

Finally, a number of staining methods are available (table 4), but the best laboratory techniques to use for the diagnosis of malignancy in bronchoalveolar lavage fluids are undetermined.

Table 2. – Diagnostic yield of bronchoalveolar lavage in lung cancer

Contributor	[Ref.]	No. of cases	No. with both BAL and diagnosis of cancer	No. of cases positive by BAL	% of cases positive by BAL
STRIZ*		471	430	225	52
WORTH*		146	99	37	37
BAGLIN	[262]	46	21	13	62
PIROZYNSKI*		124	124	44	35
LINDER	[229]	421	35	24	69
SCHABERG	[247]	31	21	3	14
Total			730	346	
	For sites mean = 45 For cases mean = 47				

*: unpublished results

Table 3. – Diagnostic yield for BAL in lung cancer

Cell type		% Yield
Bronchoalveolar cell carcinoma	11/12	92
Small cell	10/35	32
	2/3	
Squamous	0.9/49	27
	0.7/10	
Adenocarcinoma	11/20	66
	12/15	
Large cell	0/5	25
	3/7	

Data are reported for the various series available expressed as number of cases positive by BAL/number of cases of proven cancer undergoing BAL

Table 4. – Methods for the diagnosis of malignancy by bronchoalveolar lavage

Lavage technique: Lavage affected segment (CT may be helpful)		
Options*: "bronchial" and "alveolar" specimens for separate processing volume prior to/after brushings and biopsies		
Sample processing options*:		Smears Cytocentrifuge preparations Membrane filter preparations Cell pellets embedded in paraffin
Stains:	Routine*:	Papanicolaou Wright-Giemsa Haematoxylin and eosin
	Special:	Monoclonal antibodies for tumour markers

*: the "best" choice is undetermined; CT: computerized tomography.

A second limitation of lavage is that the cytological diagnosis of malignancy does not always correspond to the histologic pattern [253]. Thus, in the series of Linder, cytology agreed with biopsy in only 80% of cases. The major difficulty was in distinguishing large cell undifferentiated carcinoma from adenocarcinoma. A similar problem occurs with the severe dysplastic changes that can develop in airway epithelial cells in a variety of clinical circumstances including pneumonia, viral infections and following chemotherapy. These severe dysplastic changes can be very difficult to distinguish from malignant changes. These limitations of cytological methods must be considered when bronchoalveolar lavage is used in the diagnosis of lung cancer.

Several contributors to the current report have performed large series of bronchoalveolar lavage and have made a diagnosis of malignancy only very rarely. This has contributed to the impression that BAL has limited use in the diagnosis of cancer.

There are several reasons which may explain the low diagnostic yield at these centres: 1) case selection may have been very different at different centres; 2) pulmonologists interested in performing bronchoalveolar lavage for specific research goals may not have processed lavage specimens in a manner to maximize yield for malignancy. Some investigators, for example, throw away the first aliquot returned, which is relatively enriched for bronchial material. For malignancies originating in the bronchial tree, this may represent the material with the highest diagnostic yield. In addition, many investigators filter the fluid through loose-weave gauze in order to remove mucus. Malignant cells are often present as clumps and may be removed by such filtration procedures. Finally, many investigators have performed the procedure in patients with malignancy in order to investigate immunological abnormalities in these patients. They have intentionally lavaged sites not affected by the cancer. Thus, the relatively low diagnostic yield found by many investigators who have performed lavage for reasons other than to obtain diagnostic material, may reflect the interests of specific investigators rather than the utility of lavage to obtain material diagnostic of malignancy.

A number of tumour markers have been studied in bronchoalveolar lavage [246, 263]. While there is considerable interest among investigators in such markers, none has proved to be diagnostic. Thus, the use of these markers must be considered a research tool at present. Whether these markers will be helpful in following patients on a therapeutic protocol for malignancy is an interesting, but as yet unresolved, question. One investigator has suggested that cytological assessment of malignancy can be used for a similar purpose. Again, this must be considered a research undertaking. However, inasmuch as bronchoalveolar lavage might provide a means to assess efficacy of novel therapeutic strategies in lung cancer, it may become an important adjunct in clinical studies.

There is also a considerable interest in studying abnormalities in the patient with cancer. As such, a number of studies of bronchoalveolar lavage parameters have been undertaken in these patients. While these studies promise to provide some information as to why certain individuals develop malignancy and, perhaps, why these patients have increased incidences of lower respiratory tract infections, these studies are research studies.

It is difficult to summarize current consensus regarding the use of bronchoalveolar lavage for the diagnosis of lung cancer. Current practices vary from never performing this procedure for this indication to routinely performing this procedure for this indication. At institutions where this procedure is never performed, there is, obviously, no diagnostic yield associated with bronchoalveolar lavage. Centres where bronchoalveolar lavage has been found to be useful in the diagnosis of lung cancer are those where the procedure can be performed readily, the samples can be processed easily and trained personnel are available for the routine analysis of the specimens. In such a favourable setting, it would seem reasonable to include bronchoalveolar lavage in the diagnostic routine used to evaluate patients for lung cancer. This is particularly so considering that the procedure has exceedingly low morbidity, and the increased cost over performing a bronchoscopy with other diagnostic procedures is relatively low.

Other therapeutic applications of BAL

WLL has been proposed in the treatment of some other pulmonary disorders such as alveolar microlithiasis or exogenous lipoidosis, with some clinical but without any objective functional or radiological improvement [282].

In cystic fibrosis (CF), the benefit of WLL is also difficult to evaluate. It was expected that periodical repeated WLL could, if not arrest, at least slow down the progressive deterioration of lung function caused by the accumulation of bronchial secretions [289, 290]. Some authors have proposed WLL using antifungal drugs as a local treatment of aspergillosis, a frequent complication of CF [290]. This requires further investigation.

Conclusions

The therapeutic value of BAL is now perfectly established in alveolar proteinosis, which remains the only definite indication of this procedure. In other lung disorders, this technique still has a risk/benefit ratio which does not argue for its use in routine clinical practice. Its indication should be discussed for each patient and performed by an experienced staff in the context of an intensive care unit.

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